

Pattern of Clues

Evidence of Distinct DNA Methylation in Newborns of Smoking Women

When pregnant women smoke, it affects their children's health well beyond the womb, increasing their risk of obesity, cancer, respiratory illness, and lung disorders. To study the roots of these associations, a team of investigators assessed DNA methylation across more than 470,000 cytosine–guanine dinucleotide (CpG) sites in cord blood samples and found a highly significant association between maternal smoking and methylation [*EHP* 120(10):1425–1431; Joubert et al.]. They observed differential methylation not only in genes known to be involved in the detoxification of tobacco smoke but also in one gene not previously associated with smoking.

The team tested 1,062 cord blood samples from the Norwegian Mother and Child Cohort Study (MoBa). The average age of the MoBa mothers was 29.5 years, and 12.8% had blood plasma levels of cotinine (a nicotine metabolite) consistent with active smoking. The scientists analyzed 473,844 CpG sites across the genome using the 450K BeadChip assay platform and found differential methylation of 26 sites mapped to 10 different genes for smoking versus nonsmoking mothers. They then replicated these findings in a sample of 36 mothers from the North Carolina–based Newborn Epigenetics Study (NEST), half of whom reported smoking and half of whom did not.

Four of the 26 CpG sites were located on the aryl-hydrocarbon receptor repressor (*AHRR*) gene on chromosome 5, and several sites were just upstream of cytochrome P450 isoform *CYP1A1* on chromosome 15. Both genes are known to be involved in the aryl hydrocarbon receptor signaling pathway, which detoxifies polycyclic aromatic hydrocarbons, including those found in tobacco smoke. The MoBa cohort showed increasing methylation with cotinine levels in cord blood for one CpG site in the *AHRR* gene.

Growth factor independent 1 transcription repressor (*GFI1*) on chromosome 1 is a gene not previously associated with tobacco smoke, but in this study eight CpG sites on this gene were differentially methylated in children of smokers. *GFI1* plays a key role in several developmental processes, including the formation of



Researchers detected differential methylation of four genes in association with maternal smoking.

blood cells, pulmonary neuroendocrine cells, and the inner ear. The gene also plays a role in cellular differentiation, proliferation, and oncogenesis.

The scientists found remarkable similarity in their results between the MoBa and NEST cohorts, both in terms of which genes were differentially methylated in relation to smoking and in the direction of the associations—in other words, whether smoking was related to increased or decreased methylation at a particular CpG site. Taken together, these two studies provide strong evidence for DNA methylation contributing to the effects of maternal smoking in children.

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Element of Surprise?

Rice as a Source of Arsenic in Children's Diets

Last winter, the discovery of arsenic in foods containing organic brown rice syrup, including toddler formulas, made headlines. Members of the same research team now report higher urinary arsenic concentrations in children who eat any type of rice than in children who don't, suggesting this food may be an important source of arsenic exposure for children in the United States [*EHP* 120(10):1418–1424; Davis et al.].

Rice is an economic, nutritious staple food consumed around the world, and its popularity is growing in the United States. In addition, rice flours, syrups, and other products are widely used in processed foods. But rice plants are especially well suited to accumulating arsenic from the soil in which they grow. The arsenic content of rice varies widely depending on where it was grown and how it was processed.

In the current study, researchers examined data for 2,323 children who participated in the National Health and Nutrition Examination Survey between 2003 and 2008. They compared concentrations of arsenic in the urine of children estimated to have eaten at least a quarter cup of cooked rice during the previous 24 hours and the urine of children estimated to have eaten none. These estimates were

based on children's consumption of rice itself plus foods that contain rice-based ingredients.

"Rice eaters" had a median urinary arsenic concentration of 8.9 µg/L compared with 5.5 µg/L for "non-rice eaters." After adjusting for possible confounding factors and excluding children who had eaten seafood (a major source of a form of arsenic that is considered nontoxic) during the past 24 hours, the study found that urinary arsenic concentration increased 14.2% with every quarter-cup increase in rice that the children ate. The association was greater in children aged 6–11 years than in children aged 12–17 years, suggesting possible metabolic or dietary differences between the two age groups.

One limitation of this study is that the researchers assessed all forms of rice combined and did not examine the impact of specific types of rice on urinary arsenic concentration. Another is that estimates of the rice content in each processed food may have been off.

There is some evidence that high levels of arsenic exposure during childhood are associated with neurobehavioral problems as well as cancer and lung disease later in life. However, further research is needed to understand the health effects of exposures like those observed in this study.

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